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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,631	01/31/2007	Osman N. Ozes	INTMU.036NP	4057

20995 7590 06/21/2007

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
06/21/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/574,631	OZES ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 01 April 2006 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS 1-17 ARE PRESENTED FOR EXAMINATION

Applicants' submissions filed up to the date of the present Office action, May 21, 2007, have been received and entered into the application. The present application has not been amended and an Information Disclosure Statement has not been filed. The present action on the merits of the claims is based on the above referenced papers.

Claim Interpretation

In the present specification at page 7, paragraph [0034], it is set forth that "[a]s used herein, the term "pirfenidone analog" means any compound of Formula I, IIA or IIB below". This definition is reasonably clear, deliberate and precise, (see MPEP § 2111.01). The Examiner adopts Applicants' definition as controlling.

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

I Claims 1-3 and 12-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of administering an effective amount of the claim designated compound(s) to an individual in need of treatment for a specifically identified disease or disorder, (e.g., the disorders of claims 4, 5, 9, 10 and/or 11), does not reasonably provide enablement for such administration where the particular therapeutic objective has not been identified. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope

with these claims because of the reasons set forth below regarding the state of the art concerning the concept of a panacea.

This point of rejection may be overcome by amending the claims to include a Markush grouping of the disease states specifically identified in the present specification.

II Claims 6-8 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the treatment of any one or more of the cancers disclosed in the present specification at pages 25-26, paragraphs [00107] - [00110], does not reasonably provide enablement for the treatment of cancer in general, which embraces the treatment of *all* cancer known to the artisan. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

This point of rejection may be overcome by amending the claims to recite the particular type of cancers identified in the present specification, (pages 25-26, paragraphs [00107] - [00110]).

III Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the objective of "treating" where treating means inhibiting the disease or arresting the development of the disease or relieving, ameliorating or causing the regression of a disease, does not reasonably provide enablement for a method of preventing the disease. In the present specification, bridging pages 2-3, Applicants have indicated that by the use of the term "treating", they intend such to encompass prevention, where the disease if kept from *ever* occurring. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Burden on the Examiner for Making a Rejection Under 35 U.S.C. § 112 First Paragraph

As set forth in *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971):

"[A] [s]pecification disclosure which contains teaching of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contain therein which must be relied on for enabling support*; assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in specification is truly enabling." (emphasis added).

I Respecting the above rejection of claims 1-3 and 12-17, the claims as filed are not limited to a treatment directed to any particular disease/condition. Therefore, giving the claim terminology a broad and reasonable interpretation, (i.e., see MPEP § 2111), the claims encompass the treatment of the host for *any* therapeutic purpose. As per the court's decision of *Marzocchi*, the Examiner doubts the objective truth thereof because the art is unaware of any agent, or combination of agents, which is effective for treating all disease conditions, i.e., a panacea. Lacking knowledge of such, practicing the claimed method in the manner disclosed by Applicants would not imbue the skilled artisan with a reasonable expectation that all disease conditions could be treated in a mammal taking the claimed composition. Given that the art fails to recognize, and Applicants have failed to demonstrate, that all disease conditions could be treated in a mammal being administered the claimed composition, the skilled artisan would be faced with the impermissible burden of undue experimentation in order to practice this

embodiment of the claimed invention.

The following references are relied upon in support of the Examiner's position that panaceas are not recognized in the art: Kumar (cited by the Examiner, abstract only) teaches "The role of melatonin in organisms physiology has now been widely recognized, and the wealth of information accumulated in the past two decades indicate it to be the best hormone candidate to be investigated for a universal panacea." (penultimate and last line of the abstract); Oka et al. (cited by the Examiner, abstract only) teaches "At the present time, however, there is no single panacea. To achieve the maximum preventive and therapeutic effects with the minimum toxicity, two or more immunosuppressive drugs are used appropriately in combination, taking the mechanisms of action of each into consideration (penultimate and last line of the abstract); Smith et al. (cited by the Examiner, abstract only) teaches "[hormone replacement therapy] is not a panacea for an unhealthy lifestyle." (line 11 of the abstract); and Rickels et al. (cited by the Examiner, abstract only) teaches "Anxiolytics are not a panacea, but only tools to allow the patient to help himself or herself." (lines 11-12 of the abstract).

II Respecting claims 6-8, this rejection is deemed proper after the application disclosure and claims were compared under the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The Examiner's findings based on such comparison are as follows.

The factors referenced above include:

1) Nature of invention;

2) State of the art;

3) Level of ordinary skill in the art;

4) Level of predictability in the art;

5) Amount of direction and guidance provided by the inventor;

6) Existence of working examples;

7) Breadth of claims; and

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

1) Nature of the invention.

The claims encompass/are directed to treating cancer in general.

2) State of the art.

The state of the art is well developed with regard to the treatment of specific cancer or tumor types, and the artisan recognizes "cancer" as not being one disease, but rather a group of more than 100 different and distinctive diseases with almost as many recognized chemotherapeutic regimens effective therefor, (see Cecil Textbook of Medicine, discussed *infra*). Cancer can involve any tissue of the body and have many different forms in each body area. Most cancers are named for the type of cell or organ in which they originate. If a cancer spreads (metastasizes), the new tumor bears the same name as the original (primary) tumor. The state of the art of cancer therapy, however, is quite underdeveloped for a treatment of all known cancers with either a single or a combination of chemotherapeutic agents . In particular, the artisan is unaware of any anti-cancer or anti-tumor agent, or combinations thereof, that is effective against all known cancer types. The Cecil reference (cited by Examiner on the attached form PTO-892),

clearly shows that for the various known cancer types, there is not one specific chemotherapeutic agent or agents that is effective for each and every type of cancer or tumor, which is the subject matter encompassed by the present claims, (see Cecil at page Table 198-5 at page 1065; Tables 198-6 and 198-7 at page 1066; Table 198-8 at page 10684 and Table 198-9 at page 1071).

3) Level of ordinary skill in the art.

The level of ordinary skill in the art is high and would include the skill possessed by a person holding a doctor of medicine degree. However, given the state of the art as set forth above, the artisan is currently unaware of any one particular anti-cancer agent, or a combination thereof, that is effective in treating all known types of cancer.

4) Level of predictability in the art.

The lack of significant guidance from the present specification or prior art with regard to the treatment of all cancers in a patient with any known anti-cancer formulation imparts a significant degree of unpredictability in practicing the invention as presently claimed.

5) Amount of direction and guidance provided by the inventor.

The guidance given by the specification is to generally administer the claimed composition to treat cancer broadly. Specific cancers are identified at pages 25-26, paragraphs [00107] - [00110] of the present specification and this disclosure would well enable the artisan to treat these cancers with the claimed active agent(s).

6) Existence of working examples.

The present specification is devoid of any example showing the treatment of all cancer types or a sufficient number of different types of cancer which would provide a reasonable foundation for concluding that all types of cancers could be treated.

7) Breadth of claims.

The complex nature of the subject matter to which the present claims are directed is exacerbated by the breadth of the claim. The claims are extremely broad due to the vast number of possible cancer/tumor types represented by the term "cancer".

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with this claim. Applicants have failed to provide guidance and information to allow the skilled artisan to ascertain that the present active agent is effective against all types of cancer. The limited enablement for the specifically named cancers is noted, but does not support a conclusion that all cancers could be treated.

Here, the objective truth of the statement that cancers of a non-restricted nature could each be successfully treated is doubted because the art teaches that, at best, only certain types of cancer may be treated with only certain types of compounds or combinations thereof. Given this, the treatment of all known cancers is merely a possibility and not a treatment outcome that could be accomplished with a reasonable degree of certainty or without a burden of undue experimentation, i.e., determining for which cancers the claimed composition could treat.

Accordingly, for the above reasons, claims 6-8 are deemed properly rejected.

III The burden of enabling the prevention of any or all and even one particular disease would be much greater than that of enabling the treatment of such where the treatment is intended to achieve any effect other than the absolute outcome of keeping a disease from ever manifesting as such. In the instant case, the specification does not provide guidance as to how one skilled in the

art would accomplish the objective of preventing any, all or even one disease or how a patient could be kept from ever being susceptible to such disease/diseases. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for preventing any diseases.

Also noted is that Applicants' claims allow for the instance where one, all or any particular diseases, could be kept from *ever* occurring in a human patient by administering a single dose of pirfenidone or an analog thereof to the human during his/her neonatal stage of development, e.g., 2 months of age, comparing pre- and post-treatment levels of a stress-activated protein kinase, ("SAPK") and adjusting the dosage of pirfenidone or an analog thereof and then administering another, single dose. That is, with but two (2) single doses of pirfenidone or an analog thereof, a human who has had it administered to him/her at the time of his/her birth can be kept from ever contracting any one and all diseases, including those which he/she may be genetically predisposed to, throughout the entirety of the human's lifespan. The scope of the present claims allows for such a situation, but is not enabled because the artisan would not posses a reasonable expectation of successfully accomplishing this outcome.

The Examiner will focus the following on a particular family of diseases, i.e., cancers in order to demonstrate or else show that the claimed subject matter is not enabled to its entire scope. One could extrapolate such discussion to the other diseases encompassed by the present claims, whether expressly disclosed or not.

Concerning all known cancers, it is highly unlikely, and the Office would require experimental evidence to support the contention that the claim specified actives could actually prevent such by administering, by any method, an amount of the claim specified active agents.

The specification fails to enable one of ordinary skill in the art to practice and use the claimed actives in the manner presently claimed.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Since absolute success is not reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations as complex/poorly understood as the known types of cancers, the specification is viewed as lacking an adequate enabling disclosure of the same.

Again as per *Marzocchi, Id.* Here, the objective truth of the statement that a disease or a group of diseases such as the cancers could actually be prevented is further based on the teachings of Hawks et al. (Hematology/Oncology Clinics reference cited by the examiner) which teaches throughout that cancer prevention is not developed to the point where prevention can be predicted or expected with a reasonable degree of certainty.

Indeed, Hawks et al. teaches that "Nevertheless, a brief review of the proceedings from the 1984 workshop reveals that the challenges involved in translating *the promise of cancer prevention* into a clinical reality remain and indeed may now be even more complex" (page 809, above the heading "Neoplasia-Process Versus Event"). Thus, the art does not recognize cancer prevention to be more than a promise of the future.

Also, factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the

presence or absence of working examples; and (8) the quantity of experimentation necessary. When the appropriate factors from those above are applied to the present application (see below) and weighed, it is the examiner's position that the present specification would only enable the skilled artisan to treat the specific diseases disclosed where "treat" is limited to inhibiting the disease or arresting the development of the disease or relieving, ameliorating or causing the regression of a disease.

(1) The nature of the invention/state of the prior art, relative skill of those in the art, the predictability in the art.

The claims are directed to methods useful for preventing any one or all diseases. The relative skill of the artisan is high, but not sufficient to have imbued one with a reasonable expectation that the claimed prevention method could be realized.

(2) The breadth of the claims

The claims encompass the prevention of any one or all diseases through the administration of the claim designated actives, such as the mere administration of the claimed actives for preventing diseases.

(3) The amount of direction or guidance presented and presence or absence of working examples.

The specification provides merely provides statements that diseases may be prevented. No experimental data is present that shows, in fact, the prevention of a single disease.

(4) The quantity of experimentation necessary.

Applicants have failed to provide guidance and information sufficient to allow the skilled artisan to ascertain how to absolutely cure, i.e., prevent any disease. Testing would be necessary

on each and every disease, or at least representative number of diseases where no expectation of success would be enjoyed to accomplish a cure therefor.

(5) The State of the Art

It appears that the etiology and progression of diseases, such as cancers, remain uncertain. In order to prevent a disease from occurring, it is believed that one would first have to have a well developed understanding of how the disease begins/progresses. Also, from the Hawk et al. reference cited above, it is shown that field of cancer prevention has not yet developed into a reality, but remains merely a possible goal.

For the above reasons, the claims are deemed properly rejected and none are currently in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Raymond J Henley III
Primary Examiner
Art Unit 1614

May 21, 2007